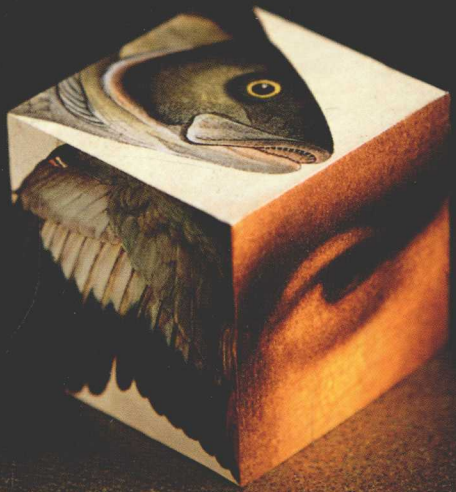
"A poet's embrace of the biological world, written with grace and intelligence, warmed by a personal story." — Alan Lightman

Chance in the House of Fate

A NATURAL HISTORY OF HEREDITY



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MARINER BOOKS

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A Natural History of Heredity

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Houghton Mifflin Company

BOSTON NEW YORK 2001

Library of Congress Cataloging-in-Publication Data

Ackerman, Jennifer.
Chance in the house of fate : a natural history of heredity / Jennifer Ackerman.
p. cm.
Includes bibliographical references.
ISBN 0-618-08287-5
1. Heredity, Human — Popular 2. Human genetics — Popular works. I. Title.
QH431 .A25 2001
599.93'5 — dc21 00-054122

Book design by Anne Chalmers
Fonts: Minion, Lucida Sans

Printed in the United States of America
QUM 10 9 8 7 6 5 4 3 2 1

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CHANCE IN THE HOUSE OF FATE

FOR MY FAMILY

I am the family face;
Flesh perishes, I live on.

—Thomas Hardy

PREFACE

THERE ARE MYSTERIES in all families. Those that arrest me, that set me back on my heels, are the mysteries of heredity—the past whispered in bone and blood; the dozens of ancestors rolled up in one skin, to be read in "curve and voice and eye," as Thomas Hardy wrote, "the seeds of being that heed no call to die" but turn up again and again on the doorstep like a ne'er-do-well uncle. It seems astonishing that a sweep of eleven generations hardly modifies the night blindness of one family or the trembling jaw of another, that fifty or a hundred years may fail to alter a familial pattern of whorled eyebrow or "wolf's" teeth, the musical genius of the Bach family, or the dimpled chin of my husband's tribe.

In the last decade or so, a startling new message has come out about the long hold of heredity. Members of the human family carry traits that have held on down the line not just for generations but for eons, traits that mock all boundaries of time and kind. Scientists probing the deep workings of organisms from yeast to humans have turned up news that despite our outward differences of life and limb, we are run by similar genes and proteins, similar cell parts and mechanisms, which have weathered evolution over ages, passing nearly intact through hundreds of millions of years of rising and falling forms. These shared molecules and routines affect nearly all the turnings of life, from birth and growth to perception and behavior.

This book is a pilgrimage to the heart of heredity. It is a natural history not in the literal sense of a systematic inquiry, but rather in the etymological sense, a telling of stories about life, lineage, chance, and fate; about family, kin, and kind. It explores both the projecting traits of the human family—the one we're born into and the one we create—and also the bigger, deeper inheritance that ties us to the rest of life in profound, even shocking ways.

• • •

I like to hang around the doorway of biological surprise. For years I have collected news of curious findings, of young spiders that eat their mothers, of a giant fungus infecting miles of Michigan forest spawned by a single spore in the last ice age, of fish with fingers, caterpillars with lungs, genes with secrets. I don't profess to worship everything, but I do harbor strange sympathies fired by such discoveries, a kind of naturalist's faith. This is the news that sweeps me away, the gnomic workings of the living order, nature's inventive jack-in-the-box surprises that shift our view of life like the sudden twist of a kaleidoscope.

Here is an item from my files. When scientists deciphered the intimate details of mating in yeast, that single-celled fungus that raises our bread and brews our beer, they got a shock. The molecule that draws two yeast cells into sex closely resembles one made by our own brain cells to regulate reproduction.

The likeness seemed a fluke at first. But then other examples popped out of the box: genes that shape the bodies of fruit flies so like our own body-shaping Hox genes that one can put a human Hox gene into a developing fruit fly embryo, and it will carry out the job of the fly's gene without a hitch; genes that shape the marvelous globe of the human eye strangely similar to those that carve the compound eye of a fruit fly; the tiny genetic mechanisms that drive our biological rhythms, keeping us in tune with the big swings of night and day, matching those in algae. So, too, do we share with other organisms the ancient genes that dictate cell death, the phenomenon that underlies metamorphosis, turning tadpoles into frogs and caterpillars into butterflies and also shapes our bodies, whittling away the webbing between fingers before birth, eliminating inappropriate sexual organs. Common to all of us, as well, is a suite of small, sturdy messenger molecules, offering clues to such mysteries as why the cells of the human brain respond to the chemical messages of the poppy plant and to the potent sexual attractants of a Himalayan deer.

What are chemicals found in the human body doing in plants, fungi, bacteria? How can genes that shape a fruit fly be near twins of my own?

Disparate organisms, it seems, are more radically alike than we ever imagined. Our deepest selves—our very cells and molecules—are alive with reminders of old, enduring connections with other creatures, resemblances that run right down to the root of the tree of life. These items of shared inheritance have formed a library of wonders in my mind's eye. That there is a certain sameness among life's various forms follows from the no-

tion that we all arose, ultimately, from a common ancestor. We are shaped by fate, by what came before. But life has chanced to venture in wildly different directions. In learning to suck energy from sunlight and in swallowing shocking amounts of oxygen, in heaving up from the beneficent chemical crucible of the sea and in exploring leafy interiors and desiccated desert, life has split into discrete identities, strewn about fresh designs, unimaginably varied feet, teeth, tongues, antennae, wings, leaves, brains.

In this world of dreamlike change, the lexicon of genes, like human languages, is thought to evolve along unreturning tracks. We know that nature is constantly making random changes in almost all genes, and that two species that diverged from a common ancestor hundreds of millions of years ago are likely to have accumulated a lot of little alterations. As eons pass, so do variants of genes, vanishing on the same wind that took the tyrannosaurs. It seems strange and wonderful that among organisms so spirited with individuality and detail—pepper frog, salp, dragonfish, basset hound—there should be so much solid common ground.

Over the last few years I have wandered the body, looking for these legacies and slim continuances, seeking to ferret them out of their holes and sun them a little, to brush their surface in places, give them a stab or pinch them to the bone if I could. I have tracked the labyrinthine world of laboratories, too, asking about the molecular bricks that underlie the splendid medley of living forms: what makes them work so beautifully that they have demanded little change in hundreds of millions of years? What happens if they go awry? If organisms of such diverse stripes are made of similar genes, how is newness born in the world?

By exploring this deep-down world, I hope to create new shelves in my mind for the recent profusion of genetic discoveries, the news of the sequencing of genomes from the tubercle bacillus to *Homo sapiens,* the findings of genes linked with cancer, Alzheimer's disease, migraine, and baldness, passed down from father to son, grandmother to granddaughter; genes affecting intelligence, sexual preference, spatial ability, anxiety, sense of well-being—some of them discovered in small, so-called model organisms such as worms, fruit flies, mice.

What is a gene, anyway? Are there genes "for" particular traits? Are the letters DNA and RNA an Open Sesame to all the familial secrets of life? Can we starve all of nature's mysteries into molecular oneness, explain the fruit solely by its root?

And what does one make of the notion that our genes mirror those in

yeast? Two decades ago scientists discovered that humans and chimpanzees appear to have in common about 98 percent of their DNA. Chimps are one thing, yeast is quite another. The news that, when it comes to molecules, we are so perilously close to our tailed, finned, and spoorish brethren goes against the stories I grew up on, biblical tales of human supremacy and uniqueness, stories of how I was "fearfully *and* wonderfully made," as it is written in the Psalms, to get up before the sun and buy a river, to buzz above all creatures, "over the fish of the sea, over the fowl of the air, over the cattle, over every creeping thing that creepeth upon the earth."

> Fear not therefore: ye are of more value than many sparrows.
> (Luke 12:7)

We have for so long picked ourselves out from the horde of other creatures, reckoned ourselves the peak and point of nature's whole history. What to do now, with this news of our deep-down similarity, our profound kinship, with "lowly" organisms?

The physicist Michio Kaku once wrote that finding the key to weather and seasons required a leap into another dimension, up into outer space. Understanding humanity's place in the matrix of life requires just such a leap, but downward, into the diminutive world of genes and cells.

Raised as I was on gerbils and birds, on the love of the whole organism, not its microscopic parts, I find it a stretch to descend into the darkness of a molecular world. I know my bats, weasels, and wood frogs far better than I do the crabbed atoms of a hemoglobin molecule. I am far more comfortable exploring the elements of the violet family than those of the periodic table. The human mind may have mastered the black hole and the quark, but most of us have difficulty grasping the very big and the very small. We tend to think easily only of things on our own scale, midway between the atom and the sun. The first microscopists, confronted with the bizarre creatures swimming beneath their lenses, sought desperately to see bodies like their own, searched for sign of head or tail, denied as long as they could the many orifices and multiple stomachs, the brainless chunks of transparent flesh. So, too, we may seek in vain the familiar in the minute parallel planet of genes and proteins.

To make things worse, the language of this world veers into the cold domain of chemistry, where the common nouns are "nucleic acids" and "amino acids"; the common verbs, "regulate," "synthesize," and "catalyze." One scientist grappling with the absence of a precise definition for the term

"gene" offered this to snarl the brain: "It is the nucleotide sequence that stores the information which specifies the order of the monomers in a final functional polypeptide or RNA molecule, or set of closely related isoforms."

But despite the dull terminology used to describe it, the cosmos of molecules and cells has surprising beauties and minute dramas every bit as beguiling as those of a bushmaster or a Bengal tiger. In DNA, proteins, even in the molecules of water encapsulated in our cells, are shapely details, beautiful clues that hold the key to everything from the acuity of the eye to the memory of the immune system. In their daily workings are tales of seduction, compromise, duplicity, deception, stubbornness, art, magic, death.

I first learned of the Hox body-shaping genes when I was a few months pregnant with my second child. The idea that the molecular mechanisms shaping my baby's growth were the same as those fashioning the fruit fly I found oddly comforting. Think of all the bending and breaking in the boughs of life. The notion that species as remotely related as humans and flies are shaped by the same genes—genes that have slipped in and out of the Cambrian, the Devonian, the Permian, the Pleistocene, requiring little revision in all that time—suggests that they must perform their task beautifully and will not easily be wrenched off course.

Fish, fruit flies, wondrous babies: we may be a feast of distinct entities, but we share the odd economies of nature from birth to death. I'm thrilled to find that we're connected with other organisms, not by something as vague or slippery as animal nature, but by a strong ribbon of measurable molecules, molecules so alike that they can be swapped between species separated by half a billion years of evolution.

I think our minds are built for the pleasure of discovering likenesses or links between vastly different things. It is why we delight in learning that the words "fate" and "symphony" share an ancient root meaning "to speak"; that the opening of Beethoven's Fifth neatly repeats the call of the white-breasted wood wren; that pointing a single finger to draw attention to something of interest is bound tightly to the learning of language. (The earlier a baby extends a demonstrative digit, the more words he or she will know by the age of two.) It is why we love syzygies and rhymes and why we are undone by Romeo's words when he finds Juliet in the tomb and thinks her dead: "Death hath suckt the honey of thy breath." It is why we believe Emerson when he tells us that "the world is a Dancer; it is a Rosary; it is a Torrent; it is a Boat; a Mist; a Spider's snare."

The language of science holds a hunch here. Though some scientific

terms are Latinate and pompous, or simply weedy (*deoxyribonucleic acid,* for instance, a great millipede of a term that puts the mind off with its literalness), there are other terms—pithy, germinal, long-lived, and prophetic—that link the unlike and suggest the blooming mysteries of both language and life. The word "gene" goes back to an Indo-European root word that meant beginning and birth. This gave rise to the Old English *gecynd,* meaning family, kin, or kind. The Greek and Latin variants blossomed into a bunch of *gen* words with a multitude of jobs: genus, genius, gender, gentle, generous, generation, genealogy, genesis. One Latin stem became *gnatus,* unfurling into innate, native, natural.

That so short and spare a word as "gene" would persist through the revolutions of language and pop up in all these new, masterful forms impresses me. So do these shared ancestral genes, which are something like word roots. Knowing them is a way of prizing what is essential in our common heritage. That we are still abob with these ancient bits of biological wisdom, that they have endured over eons in creatures as genealogically distant as worms and widowed aunts, is to me as much a cause for celebration as a Bach cantata or bird song.

These fragments of shared biology arose by chance and became fate. I have come to think of them as points of entry or small portholes through which to view the natural history of heredity. Or, perhaps, like the scriptural mustard seed cast into the family garden, from which one might draw radii to every corner of nature.

This book is a tracing of those radii. It is a journey in four parts, starting with the roots of all flesh, the inherited molecules that keep our bodies and those of other mortals alive and thriving; then moving to the generation of our being as single, sentient organisms, from our beginnings in sperm and egg—those seeds of inheritance—to the birth of bodies with vision and the capability of sex. Thence to our relations with other living things, how we recognize, compete, and conspire with them in the deepest, most intimate ways to make something more useful, more skillful, more beautiful than what we might have made alone. And finally to our common passage through time, from the immediate tick of the present, by which our bodies stay in tune with the swing of sun and moon, to our long passage out of the past, from earliest beginnings.

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PART I

ROOTS

Root, from Indo-European *werād,* branch or root. The inner core or essential nature of something; a source or origin; an antecedent or ancestor.

1

GENEALOGY

WHY IS IT so strange and sweet to ponder a family tree? There's the chance to peer beyond one's personal limits, to spot from the mast a sea of unremembered relatives. Or to hunt up a lost connection with a distant great-grandmother, to delve into the mystery of her existence in her old home country. There's the hope for pride of birth or social credentials or a sense of rootedness, an antidote for those plagued by mobility, by birdly migrations over one ocean or another, between country and town, up or down the social ladder. Then there's the slim but tantalizing possibility of pecuniary gain in uncovering a link with a relative of large estate — though this is often a mixed blessing, *damnosa hereditas,* the Roman jurist Gaius called it. Come for your inheritance, says a Yiddish proverb, and you may have to pay for the funeral.

In my own family tree, I've relished the weird weaving of ancestral names — Doerfler, Dresen, Homann, Huck, Koeppel, on one side; Goldfarb, Dunkelmeyer, Blank, on the other — names of dimly recollected forebears who watched the skyline of New York from the fourth-class deck of a steamer. I've also applauded the surprises in my immediate family, the four girls defying the odds of sex ratio and, especially, the exotic tendril of our fifth sister, Kim, adopted by my parents from a Korean orphanage when she was four, whose own biological roots remain a kind of Siberia.

Apart from satisfying a curiosity about one's origins or a yearning for old connections, apart from settling the matter of estate, a practical use of genealogy is to sort out the hereditary components of disease. When I was entering puberty, my mother took my sisters and me to a genetic counselor to discuss our risk of bearing defective babies. Ten years earlier my youngest sister, Beckie, had come into the world with microcephaly and profound mental retardation.